I. Remarks

Claims 1-30 are currently pending. Claims 1, 3, 12, and 13 are under consideration pursuant to a restriction requirement.

A) Claims 12 and 13 have been amended with this response. The amendment to claim 13 corrected a typographical error by correcting the misspelled word "presenece" to the correctly spelled "presence". The amendment to claim 13 allows claim 1 to provide proper antecedent basis. Support for this amendment is found throughout the instant specification page 3, lines 11-20 and page 20, lines 13-26. Therefore, these amendments do not add new matter and Applicants respectfully request their entry.

B) Applicants note that a new oath or declaration under 37 C.F.R. §1.67(a) is required in the instant application. Due to the geographical location of the instant inventors, this oath will be submitted in a separate filing from this communication when it has been fully executed.

C) The specification has been amended with this response to correct errors in the specification. In particular, these amendments correct various spelling errors and correct improperly demarcated trademarks so that, to Applicants' best knowledge, they are now properly demarcated. Therefore, the amendments made to the specification do not add new matter. Applicants respectfully request their entry.

II. Claim Objections

A) Claims 1, 12, and 13 stand objected to because claim 1 is drawn in the alternative to the subject-matter of non-elected inventions.

Applicants respectfully note the Office's objection to claim 1. Once allowable subject matter has been identified, Applicants will amend the instant claims to limit them to the examined subject matter.

B) Claim 12 stands objected to because of an inadvertent misspelling "presenece". Applicants have amended claim 12 to correct the misspelling with this response. Therefore, withdrawal of this objection is respectfully requested.

III. Claim rejections under 35 U.S.C. § 112

Claim 13 stands rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the

invention. In particular, claim 13 is allegedly indefinite because the limitation, "the lung cancer", finds no antecedent basis in either of claims 1 or 12. Applicants respectfully traverse.

Applicants have amended claim 13 with this response, which renders this rejection moot. Withdrawal of the rejection is therefore respectfully requested.

IV. Claim rejections under 35 U.S.C. § 102(b)

Claims 1, 3, 12, and 13 stand rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Mooi et al. (Histopathology, 1988, 13 (3): 329-337) as evidenced by Wilkinson et al. (Science, 1989, 246 (4930): 670-673). In particular, the Office has concluded that Mooi et al. anticipates the instant claims by teaching the detection of the PGP9.5 protein via immunohistochemistry in 11 lung tumor samples. Applicants respectfully traverse.

Mooi et al. cannot anticipate the instant invention because, while it demonstrates that certain lung tumors are neuroendocrine in nature as indicated by neuronal marker staining, it does not teach or suggest that PGP9.5 over-expression is indicative of a neoplastic condition in lung cells as instantly claimed. Rather, Applicants were the first to recognize that PGP9.5 over-expression is a marker for a neoplastic condition in lung cells because Applicants discovered that PGP9.5 is present in lung cancer cells regardless independent of neuronal differentiation.

Mooi et al. teaches the use of several neuronal markers, including PGP9.5, to confirm whether certain lung tumor samples were neuroendocrine in nature (Mooi et al., page 336, lines 1-6.) Due to the positive staining of these markers observed in the 11 tumors evaluated, Mooi et al. determined that all 11 were indeed neuroendocrine tumors (Mooi et al., page 336, lines 14-15.) The reference does not teach or suggest the use of PGP9.5 as a tumor cell marker. It merely demonstrates the use of PGP9.5 in a panel of neuronal markers to establish the neuroendocrine status of the 11 tumors selected for the study. In contrast, Applicants recognized PGP9.5 as a marker for a neoplastic condition in lung cells because they determined that PGP9.5 is not simply a neuronal marker. Rather, Applicants recognized that PGP9.5 over-expression occurs in lung cancer cells both neuroendocrine and non-neuroendocrine in nature.

Lung cancers often have features of neuronal differentiation. Therefore, Applicants evaluated whether or not the PGP9.5 over-expression discovered through SAGE analysis simply reflected the neuroendocrine status of the cancer cells tested. Expression levels of one of the most reliable markers of neuroendocrine differentiation, hASH1, and PGP9.5 were simultaneously evaluated in a number of

cancer cell lines. (Expression of hASH1 is essential for neurodifferentiation of the lung.) Applicants discovered that PGP9.5 protein was abundantly expressed in nearly all cancer cell lines tested (including small-cell lung cancer cells and non-small cell lung cancer cells) independent of their hASH1 status (see the instant specification at Figure 3B and page 36, lines 8-14.) PGP9.5 was detected in both the neuroendocrine (hASH1 positive) lung cancer cells and in the non-endocrine (hASH1 negative) lung cancer cells. It was present in lung cancer cells independent of neuronal differentiation. Based on this independent and frequent occurrence of PGP9.5 over-expression, Applicants recognized that PGP9.5 is a marker useful in diagnosing the neoplastic condition of a lung cell. Prior to the instant application, PGP9.5 was, as demonstrated by Mooi et al., only considered diagnostic as a neuronal marker.

Therefore, Mooi et al. cannot and does not anticipate the instant diagnostic method claimed. Mooi et al. only teaches that the 11 lung tumors tested were neuroendocrine in nature following immunohistochemical staining of a panel of neuronal markers, which included PGP9.5. As such, Mooi et al. cannot provide a teaching demonstrating that PGP9.5 is over-expressed in both neuroendocrine and non-neuroendocrine lung cancer cell so as to identify it as a marker for the neoplastic condition of a lung cell. Applicants respectfully assert that Mooi et al. does not anticipate the instant invention. Withdrawal of the rejection is therefore respectfully requested.